

OVERVIEW OF THE ACTION¹

1. NeoGenomics expressly denies that any NeoGenomics product or any of its activities fall within the alleged scope of any claim of U.S. Patent Nos. 11,530,454 (the “’454 Patent”) and 11,519,035 (the “’035 Patent”) (collectively, “Asserted Patents”) or otherwise constitute infringement. NeoGenomics admits that the Complaint purports to state an action for infringement of the ’454 and ’035 Patents. Except as expressly admitted herein, NeoGenomics denies each and every allegation in paragraph 1 of the Complaint.

THE PARTIES

2. NeoGenomics admits that Natera is a corporation organized and existing under the laws of the state of Delaware.

3. Paragraph 3 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 3 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

4. Paragraph 4 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 4 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

5. Paragraph 5 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 5 contains factual allegations, NeoGenomics is without

¹ For the Court’s convenience, NeoGenomics generally adopts the headings used in Natera’s Complaint. In so doing, NeoGenomics does not admit that the headings are accurate, and reserves the right to contest any statement or characterization set forth under them. To the extent the headings constitute allegations requiring a response, they are denied.

knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

6. Paragraph 6 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 6 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

7. Denied. NeoGenomics specifically denies that it has committed the alleged acts of infringement or that NeoGenomics “used Natera’s patented cfDNA technology.” NeoGenomics further denies that the Asserted Patents claim “patented inventions.”

8. NeoGenomics admits that it is a corporation organized and existing under the laws of the State of Florida. NeoGenomics further admits that it operates laboratories throughout the United States, including in Durham, North Carolina.

9. NeoGenomics admits that it is a corporate affiliate of both Inivata, Inc. and Inivata Ltd. (collectively, “Inivata”). NeoGenomics further admits that it is a wholly owned subsidiary of NeoGenomics, Inc. and that Inivata, Inc. and Inivata Ltd. are wholly owned subsidiaries of NeoGenomics.

10. NeoGenomics admits that it operates under and identifies with the trade name “NeoGenomics” and “NeoGenomics Laboratories.” Except as so admitted, NeoGenomics denies the remaining allegations in paragraph 10.

11. NeoGenomics denies each and every allegation in paragraph 11. NeoGenomics specifically denies that it has used or is using Natera’s patented technology.

JURISDICTION AND VENUE

12. NeoGenomics admits that this Court has subject matter jurisdiction over causes of action for alleged patent infringement pursuant to 28 U.S.C. §§ 1331 and 1338(a).

13. The allegation of personal jurisdiction in paragraph 13 constitutes a legal conclusion that requires no response.

14. The allegation of proper venue in paragraph 14 constitutes a legal conclusion that requires no response.

BACKGROUND

15. Paragraph 15 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 15 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

16. Paragraph 16 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 16 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

17. Paragraph 17 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 17 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

18. Paragraph 18 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 18 contains factual allegations, NeoGenomics is

without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

19. Paragraph 19 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 19 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

20. Paragraph 20 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 20 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

21. Paragraph 21 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 21 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

22. Paragraph 22 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 22 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

23. Paragraph 23 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 23 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

24. Paragraph 24 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 24 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

25. Paragraph 25 of the Complaint contains statements of opinions to which no response is required. To the extent paragraph 25 contains factual allegations, NeoGenomics is without knowledge or information sufficient to form a belief as to the truth of those allegations, and therefore denies each and every allegation in that paragraph.

Response To Allegations Regarding General Background of the Inventions

A. The '454 Patent

26. NeoGenomics admits that, on its face, the '454 Patent is entitled "Detecting Mutations and Ploidy in Chromosomal Segments," states that it was issued on December 20, 2022, and lists Natera as the assignee. As to the remaining allegations, NeoGenomics is without knowledge or information sufficient form a belief as the truth of the allegations, and therefore denies the remaining allegations in that paragraph.

27. NeoGenomics admits that, on its face, claim 1 of the '454 Patent recites:

A method for preparing a plasma sample of a subject having cancer or suspected of having cancer or useful for detecting one or more single nucleotide variant (SNV) mutations in the plasma sample, the method comprising:

performing whole exome sequencing or whole genome sequencing on a tumor sample of the subject to identify a plurality of tumor-specific SNV mutations;

performing targeted multiplex amplification to amplify 10 to 500 target loci each encompassing a different tumor-specific SNV mutation from cell-free DNA isolated from a plasma sample of the subject or DNA derived therefrom to obtain amplicons having a length of 50-150 bases, wherein the target loci are amplified together in the same reaction volume; and

sequencing the amplicons to obtain sequence reads, and detecting one or more of the tumor-specific SNV mutations present in the cell-free DNA from the sequence reads, wherein the sequencing has a depth of read of at least 50,000 per target locus.

NeoGenomics admits that claim 1 recites “single nucleotide variant (SNV) mutations,” “whole genome sequencing,” and “multiplex amplification.” NeoGenomics denies the remaining allegations in paragraph 27.

28. Paragraph 28 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 28.

29. Paragraph 29 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 29.

B. The '035 Patent

30. NeoGenomics admits that, on its face, the '035 Patent is entitled “Methods for Simultaneous Amplifications of Target Loci,” states that it was issued on December 6, 2022, and lists Natera as the assignee. As to the remaining allegations, NeoGenomics is without knowledge or information sufficient form a belief as the truth of the allegations, and therefore denies the remaining allegations in that paragraph.

31. NeoGenomics admits that, on its face, claim 1 of the '035 Patent recites:

A method for amplifying and sequencing DNA, comprising:

tagging isolated cell free DNA with one or more universal tail adaptors to generate tagged products, wherein the isolated cell-free DNA is isolated from a blood sample collected from a subject who is not a pregnant women;

amplifying the tagged products one or more times to generate final amplification products, wherein one of the amplification steps comprises targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci

in a single reaction volume, wherein one of the amplifying steps introduces a barcode and one or more sequencing tags; and

sequencing the plurality of SNP loci on the cell free DNA by conducting massively parallel sequencing on the final amplification products, wherein the plurality of SNP loci comprises 25-2,000 loci associated with cancer.

NeoGenomics admits that claim 1 recites “amplifying and sequencing,” “targeted amplification of a plurality of single nucleotide polymorphism (SNP) loci,” and “sequencing the plurality of SNP loci” conditions.” NeoGenomics denies the remaining allegations in paragraph 31.

32. Paragraph 32 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 32.

33. Paragraph 33 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 33.

DEFENDANT’S INFRINGING ACTS

34. Paragraph 34 of the Complaint purports to contain disclaimers and provisos by Natera to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 34.

35. NeoGenomics denies that its products, such as RaDaR, “apply Natera’s patented methods for preparing, amplifying, sequencing, and analyzing cfDNA to detect and monitor genes and genetic mutations associated with a patient’s cancer.” NeoGenomics denies each and every allegation in paragraph 35.

36. Paragraph 36 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 36.

37. Paragraph 37 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 37.

38. NeoGenomics admits that documents purporting to be claim charts for claim 1 of the '454 Patent and claim 1 of the '035 Patent are attached to the Complaint as Exhibits 3–4 with referenced documents contained in Exhibits 5–16. The claim charts and referenced documents contain statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in the claim charts, and further denies that Exhibits 5–16 support the allegations, opinions, and legal conclusions in the claim charts. NeoGenomics denies each and every allegation in paragraph 38.

39. Paragraph 39 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in Exhibit 3 and Exhibit 4. NeoGenomics further denies each and every allegation in paragraph 39.

40. NeoGenomics admits that it “designs, develops, makes and uses, or directs or controls the design, development, make and use of, the RaDaR assay by purposefully directing the activities at its CAP/CLIA-certified laboratory in the Research Triangle Park (RTP) located at 8 Davis Drive, Durham, North Carolina.” NeoGenomics further admits that, “this laboratory is registered to Inivata, Inc., a corporate affiliate of NeoGenomics Laboratories.” NeoGenomics admits that Dr. Siby Sebastian, Ph.D previously served as a director of this laboratory. NeoGenomics further admits that Dr. Siby Sebastian was “the Director of the NeoGenomics CAP/CLIA Clinical Laboratory at the Research Triangle Park (RTP), North Carolina.” NeoGenomics admits that its 2022 Annual Report to shareholders indicated NeoGenomics “ha[s]

a renewed focus on next-generation sequencing (NGS), minimal residual disease (MRD) technology such as RaDaR,[®] MultiOmyx,[™] and data capture and commercialization. Functions under this business include Pharma Services, as it is the tip of the spear for driving innovation in our industry, Informatics (the former Trapelo business), and centralized research and development. By centralizing the R&D function and integrating Inivata, we believe we are now well-positioned to capitalize on the innovation of Inivata while enhancing the development process for new products.”

41. NeoGenomics admits that it performs, or directs or controls the performance of, the RaDaR assay. NeoGenomics further admits that, in its published guide for patients, NeoGenomics Laboratories states that RaDaR testing is “conducted on [a] blood sample in our lab.”

42. NeoGenomics admits that it offers for sale and sells, or directs or controls the offer for sale and sale of, the Accused Assay. NeoGenomics admits that, on March 16, 2023, it clinically launched the RaDaR product for sale in the United States. NeoGenomics also admits that, in its 2022 Annual Report to shareholders, it stated that “[w]e believe NeoGenomics is well-positioned to gain market share with our NGS portfolio products, including Neo Comprehensive – Solid Tumor and Neo Comprehensive – Myeloid Disorders, as well as our RaDaR[®] assay liquid biopsy test for MRD.”

43. NeoGenomics admits that, while RaDaR is ordered through NeoGenomics Laboratories, its insurance reimbursement certifications and approvals, including MolDX, list Inivata as authorized to perform RaDaR tests. NeoGenomics further admits that the request forms for the RaDaR test report that RaDaR may be performed by Inivata. Paragraph 43 otherwise contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 43.

44. Paragraph 44 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 44.

45. NeoGenomics admits that, on July 27, 2023, it announced that RaDaR obtained Medicare coverage for cancer recurrence detection and monitoring in patients with breast cancer, including those with a personal history of high-risk stage II/III HR+/HER2- breast cancer, five or more years from diagnosis who presently do not have evidence of disease.

46. NeoGenomics admits that it had actual knowledge of the '454 Patent since at least as early as December 20, 2022 when Natera filed an infringement lawsuit in the District of Delaware asserting the '454 Patent against two corporate affiliates of NeoGenomics Laboratories, Inc.: Inivata, Inc., and Inivata, Ltd.

47. NeoGenomics admits that it had actual knowledge of the '035 Patent since at least as early as the date of this Complaint.

48. NeoGenomics denies that it has “made extensive unauthorized use of Natera’s patented technology.” The remainder of paragraph 48 of the Complaint contains statements of opinion and legal conclusions to which no response is required. To the extent a response is required, NeoGenomics denies each and every allegation in paragraph 48.

COUNT I: DIRECT INFRINGEMENT OF U.S. PATENT NO. 11,530,454

49. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

50. NeoGenomics lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 50 and on that basis denies them.

51. NeoGenomics denies each and every allegation in paragraph 51 of the Complaint.

52. NeoGenomics denies each and every allegation in paragraph 52 of the Complaint.

53. NeoGenomics denies each and every allegation in paragraph 53 of the Complaint.

COUNT II: DIRECT INFRINGEMENT OF U.S. PATENT NO. 11,519,035

54. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

55. NeoGenomics lacks sufficient knowledge or information to form a belief as to the truth of the allegations set forth in paragraph 55 and on that basis denies them.

56. NeoGenomics denies each and every allegation in paragraph 56 of the Complaint.

57. NeoGenomics denies each and every allegation in paragraph 57 of the Complaint.

58. NeoGenomics denies each and every allegation in paragraph 58 of the Complaint.

COUNT III: INDIRECT INFRINGEMENT OF U.S. PATENT NO. 11,530,454

59. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

60. NeoGenomics denies each and every allegation in paragraph 60 of the Complaint.

61. NeoGenomics denies each and every allegation in paragraph 61 of the Complaint.

62. NeoGenomics denies each and every allegation in paragraph 62 of the Complaint.

COUNT IV: INDIRECT INFRINGEMENT OF U.S. PATENT NO. 11,519,035

63. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

64. NeoGenomics denies each and every allegation in paragraph 64 of the Complaint.

65. NeoGenomics denies each and every allegation in paragraph 65 of the Complaint.

66. NeoGenomics denies each and every allegation in paragraph 66 of the Complaint.

COUNT V: WILLFULL INFRINGEMENT OF U.S. PATENT NO. 11,530,454

67. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

68. NeoGenomics denies each and every allegation in paragraph 68 of the Complaint.

69. NeoGenomics denies each and every allegation in paragraph 69 of the Complaint.

70. NeoGenomics denies each and every allegation in paragraph 70 of the Complaint.

COUNT VI: WILLFULL INFRINGEMENT OF U.S. PATENT NO. 11,519,035

71. NeoGenomics incorporates and restates by reference its responses to paragraphs 1–48 of the Complaint as though fully set forth herein.

72. NeoGenomics denies each and every allegation in paragraph 72 of the Complaint.

73. NeoGenomics denies each and every allegation in paragraph 73 of the Complaint.

74. NeoGenomics denies each and every allegation in paragraph 74 of the Complaint.

PRAYER FOR RELIEF

NeoGenomics denies that Natera is entitled to any relief whatsoever, including the relief requested in the Complaint, from either NeoGenomics or the Court. Natera’s prayer for relief should be denied in its entirety.

AFFIRMATIVE DEFENSES

NeoGenomics hereby sets forth defenses to Natera’s Complaint in order to place Natera on notice regarding applicable defenses. By listing any matter as a defense herein, NeoGenomics does not assume the burden of proving any matter upon which Natera, or any other party, bears the burden of proof under applicable law.

FIRST DEFENSE – NON-INFRINGEMENT

1. NeoGenomics has not infringed, and is not infringing directly, indirectly, willfully, or in any other manner any valid and enforceable claim of the Asserted Patents, either literally or under the doctrine of equivalents.

2. NeoGenomics hereby incorporates by reference in their entirety the non-infringement arguments and associated exhibits set forth in its forthcoming Opposition to Plaintiffs' Motion for a Preliminary Injunction.

3. By way of example, NeoGenomics does not infringe any claims of the '454 Patent because it NeoGenomics's RaDaR Assay does not directly sequence the amplicons, but includes an intervening step between multiplex amplification and sequencing the products.

4. By way of example, NeoGenomics does not infringe any claims of the '035 Patent because NeoGenomics's RaDaR Assay does not use targeted amplification to amplify tagged products.

SECOND DEFENSE – INVALIDITY

5. The asserted claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112 *et seq.*, and the rules, regulations, and laws pertaining to those provisions, including the application provisions of Title 37 of the Code of Federal Regulations.

6. NeoGenomics hereby incorporates by reference in their entirety the invalidity arguments and associated exhibits and prior art set forth in its forthcoming Opposition to Plaintiffs' Motion for a Preliminary Injunction.

7. By way of example, the asserted claims of the '454 Patent are invalid as obvious under Forshew et al., "*Noninvasive Identification and Monitoring of Cancer Mutations by*

Targeted Deep Sequencing of Plasma DNA,” Sci Transl Med 4, 136ra68 (2012) (including Supplementary Materials available at www.sciencetranslationalmedicine.org/cgi/content/full/4/136/136ra68/DC1) (“Forsheew (2012)”) and the skill and knowledge of a person of ordinary skill in the art at the alleged time of the invention of the ’454 Patent. Further, the asserted claims of the ’454 Patent are directed to patent-ineligible subject matter, namely, that they are directed to a method of detection claim that recites nothing more than an abstract, mental process implemented with a mathematical algorithm.

8. By way of example, the asserted claims of the ’035 Patent are invalid as obvious under *Parallel Preparation of Targeted Resequencing Libraries From 480 Genomic Regions Using Multiplex PCR on the Access Array™ System*, by Fiona Kaper, et al., in view of the skill of a person of ordinary skill in the art at the time of the alleged invention of the ’035 Patent, or obvious under the combination of U.S. Patent Pub. No 2009/025183 A1, titled *Amplicon Rescue Multiplex Polymerase Chain Reaction For Amplification Of Multiple Targets*, and Wang et al., *High Throughput Sequencing Reveals A Complex Pattern of Dynamic Interrelationships Among Human T Cell Subsets*, PNAS (January 26, 2010), in view of the skill and knowledge of a person of ordinary skill in the art at time of the invention. Further, the claims of the ’035 Patent are invalid as directed to ineligible subject matter, namely, that the claims recite a method of detection claim with techniques that are standard, routine, and conventional.

9. By way of example, both the ’035 and ’454 Patents are invalid for lack of written description. Asserted Claims from both patents contain terms with no support in the specification, demonstrating that the inventors did not have possession of the invention.

10. By way of example, the '454 Patent is invalid for improper inventorship. The '454 Patent fails to name Mariam Jamal-Hanjani, who described the work that appears in Example 13 in the specification in her doctoral dissertation.

THIRD DEFENSE – FAILURE TO STATE A CLAIM

11. Natera's Complaint, in whole or in part, fails to state a claim upon which relief may be granted.

12. As an example, Natera's Complaint fails to state a claim upon which relief may be granted because the claims of the Asserted Patents are invalid for failing to comply with one or more of the requirements for patentability under, including, but not limited to, 35 U.S.C. §§ 101, 102, 103, 112 *et seq.* as set forth below in NeoGenomics' Counterclaims.

13. NeoGenomics hereby incorporates by reference and restates Paragraphs 1-10 of its Affirmative Defenses as though fully set forth herein.

FOURTH DEFENSE – PROSECUTION HISTORY ESTOPPEL/DISCLAIMER

14. Natera is estopped from construing the claims of the Asserted Patents to cover or include, either literally or by application of the doctrine of equivalents, products manufactured, used, imported, sold, or offered for sale by NeoGenomics or methods used by NeoGenomics because of amendments, admissions, representations, or statements made before the USPTO during prosecution of the applications leading to the issuance of the Asserted Patents or applications related thereto, because of disclosures or language in the specifications of the Asserted Patents, and/or because of limitations in the claims of the Asserted Patents.

15. By way of example, Natera asserted to the USPTO during the prosecution of related U.S. Patent No. 11,486,008, that its alleged invention involved “performing high-throughput sequencing to **sequence the amplicons obtained in the multiplex targeted amplification**

reaction to obtain sequence reads.” Natera further asserted that “[i]n contrast to the claimed invention, Forshew’s TAM-Seq process requires a ‘*limited-cycle pre-amplification step*’ followed by ‘*individual amplification to purify and select for intended targets*’ (i.e., parallel single-plex PCR).” The assertions that Natera made in order to overcome an obviousness rejection show that the Asserted Claims require that the amplicons generated by performing a targeted multiplex amplification be ***directly*** sequenced without any intervening step.

16. Because of these assertions, Natera is now estopped from construing the claims of the claims of the ’454 Patent to cover or include, either literally or by application of the doctrine of equivalents, products manufactured, used, imported, sold, or offered for sale by NeoGenomics or methods used by NeoGenomics.

FIFTH DEFENSE – LIMITATIONS ON RECOVERY

17. Natera’s claims for damages and other remedies are limited by 35 U.S.C. §§ 287 and/or 288. Natera is barred by 35 U.S.C. § 288 from recovering costs associated with this action.

SIXTH DEFENSE – ADEQUATE REMEDY AT LAW

18. Natera is not entitled to injunctive relief against NeoGenomics because Natera is not likely to succeed on the merits, any alleged injury is neither immediate nor irreparable, there is an adequate remedy at law for any alleged injury, the balance of hardships and equities does not favor an injunction, and the public interest would be disserved by an injunction. Accordingly, Natera is not entitled to injunctive relief even if it were able to establish liability.

SEVENTH DEFENSE – NO EXCEPTIONAL CASE

19. NeoGenomics has not engaged in any conduct that would make this an exceptional case or that would entitle Natera to an award of attorneys’ fees.

EIGHTH DEFENSE – ACTIONS OF OTHERS

20. On information and belief, Natera's claims are barred, in whole or in part, because NeoGenomics is not liable for the acts of others over whom it has no control.

NINTH DEFENSE – CLAIM PRECLUSION

21. Natera is barred from bringing this action, in whole or in part, pursuant to the doctrine of claim preclusion.

22. On January 20, 2021, Natera filed a complaint in the District Court for the District of Delaware against Inivata, Inc. and Inivata Ltd. alleging infringement of U.S. Patent Nos. 10,262,755 and 10,597,709. *Natera, Inc. v. Inivata, Inc.*, C.A. No. 1:12-cv-00056-UNA, D.I. 1. On December 20, 2022, Natera filed a complaint in the District Court for the District of Delaware against Inivata, Inc. and Inivata Ltd. alleging infringement of the '454 Patent. *Natera, Inc. v. Inivata, Inc.*, C.A. No. 1:22-cv-01609-UNA, D.I. 1. Natera is barred from bringing this action, in whole or part, based on the aforementioned Delaware actions, which were consolidated on January 26, 2023. In these cases, Natera failed to assert the '035 Patent alongside the '454 Patent.

23. On September 15, 2023, Natera provided its First Supplemental Response to NeoGenomics's Interrogatory No. 4, which requested an explanation as to why Natera did not include the '035 Patent in cases mentioned in Paragraph 22, and an identification as to when Natera first had reason to believe the RaDaR assay infringed each asserted claim-in-suit.

24. In its Supplemental Response, Natera failed to provide any explanation, instead stating simply that NeoGenomics sells the RaDaR assay. Natera, in failing to diligently pursue claims under the '035 Patent and failing to explain the cause now, is precluded, in whole or in part, from pursuing such claims in the present case.

TENTH DEFENSE – INEQUITABLE CONDUCT

25. The '454 Patent is unenforceable due to Natera's inequitable conduct during the prosecution of the '454 Patent. This conduct includes a failure to include a rightful inventor and misrepresentations made regarding the prior art to overcome an obviousness rejection and a false statement in the patent application and patent itself that was exploited to improperly claim subject matter.

26. The '454 Patent claims the use of "whole exome" or "whole genome" sequencing of a "tumor sample" followed by "sequencing the amplicons" obtained by amplifying "10 to 500 target loci" in "cell-free DNA isolated from a plasma sample."

27. While the '454 Patent fails to adequately describe the claims, to the extent the '454 Patent includes any reference to an approach based on the use of "whole exome" or "whole genome sequencing," such disclosure appears solely in Example 13.

28. Example 13, however, describes a series of experiments that were conceived of not by the named inventors, but by researchers at University College London, including at least Mariam Jamal-Hanjani, who described the work that appears in Example 13 in her doctoral dissertation and contributed the research plan for the first experiment and actually performed at least part of the experiment including the whole exome sequencing step. This is clear from, for example, the figures and lists of genes referred to in Example 13, which are identical to those set forth in the doctoral dissertation of Mariam Jamal-Hanjani.

29. On information and belief, the research plan, drafted by Dr. Jamal-Hanjani, involves monitoring of cfDNA to detect minimal residual disease, which relates directly to the claim elements involving analyzing cell-free DNA to detect tumor-specific SNVs. On information

and belief, Natera scientist Dr. Robert Pelham responded with a revised draft to Dr. Jamal-Hanjani, which cited to more work by Dr. Jamal-Hanjani relating to whole exome sequencing.

30. On information and belief, Natera collected data using this research plan and reported back to UCL. Natera and UCL began collaborating on a publication based on this research plan, for which Natera requested protocols from Dr. Jamal-Hanjani.

31. On information and belief, the named Natera inventors and the individuals involved in prosecuting the '454 Patent (including, without limitation, Nishita Doshi, Tianran Yan, Luke Burton, and Limin Zheng) were aware that the disclosure set forth in Example 13 of the '454 patent was conceived of and performed at least in part by researchers at University College London.

32. These individuals were aware that researchers had conceived of and performed the work in Example 13 because Natera had been engaged in a collaboration with researchers at University College London related to precisely this work and, on information and belief, were in regular communication regarding research and development activities.

33. Yet, despite this, the Natera inventors and patent prosecution team included Example 13 in their application that became the '454 patent and then drafted claims that rely upon the subject matter of Example 13 without identifying any researchers from University College London as inventors.²

34. The Natera inventors and patent prosecution team omitted researchers from University College London as inventors because they wished to misappropriate the subject matter

² The content in Example 13 is material, which is supported by the fact that Natera specifically relied on Example 13 for support during the prosecution of at least two related patent applications. *See, e.g.*, Ex. 1 at 7 (alleging that then-pending claims 1, 16-17, 20-23 and 25 are supported by Example 13 (i.e., paragraph 0863 of the published application (US2018/0320239))); Ex. 2 at 1 (asserting that then-pending claims 1, 2, 4-8, and 10-11 derive basis from Example 13).

of Example 13 and be free to draft related claims and enforce such claims without being encumbered by University College London, which, on information and belief, Natera no longer collaborates with after having had a high-profile falling out with Charles Swanton, a leading oncology researcher who led the collaboration with Natera.

35. Specifically, at least Natera's Vice President & Chief Intellectual Property Counsel, Nishita Doshi, acted with deceptive intent by obtaining claims in the '454 Patent to subject matter for which Dr. Mariam Jamal-Hanjani is an inventor and thus University College London a proper assignee and owner. On November 22, 2022, Ms. Doshi received an email from Richard Fagan at University College London alerting Natera and Ms. Doshi that the applications for patents, including for the '454 Patent, include Example 13 from Dr. Mariam Jamal-Hanjani's thesis, and that it appears the concept of looking at a tumor biopsy sample, sequencing them (e.g. whole exome sequencing) to identify single nucleotide variants, and determining whether a particular SNV is clonal or not, are all concepts only described in that example. University College London also informed Natera in this email received by Ms. Doshi that it appears that Dr. Mariam Jamal-Hanjani should be named as an inventor and UCLB as co-assignee. Notwithstanding this notice, Ms. Doshi and the others substantively involved with this patent application and aware of Dr. Mariam Jamal-Hanjani's contribution failed to inform the Patent Office of this inventorship issue throughout the patent application process including on or after November 22, 2022, with the deceptive intent of obtaining patents that would appear to be solely owned by Natera and to deprive the Patent Office of the opportunity to even evaluate this issue, and they did not correct or withdraw the Natera inventorship oaths that were false by excluding Dr. Mariam Jamal-Hanjani. The basis for this allegation are further set forth in NeoGenomics's Opposition to Plaintiff's Motion for a Preliminary Injunction, the accompanying declaration of Dr. Brian Van Ness, and the other

evidence supporting the improper inventorship of the '454 Patent. The single most logical inference is that Natera deceived the Patent Office about UCL's involvement with the inventions with deceptive intent to gain sole ownership over this and other patents. That is further shown by the pattern of conduct alleged in this pleading

36. Natera's misrepresentation of inventors to the Patent Office was highly material. Title 35 U.S.C. § 115 provides that "An application for patent ... shall include, or be amended to include, the name of the inventor for any invention claimed in the application." Section 115 further states, "Except as otherwise provided in this section, each individual who is the inventor or a joint inventor of a claimed invention in an application for patent shall execute an oath or declaration in connection with the application." The Manual of Patent Examining Procedure ("MPEP") thus instructs examiners to reject applications with improper inventorship. *See* MPEP § 2137.01 (explaining that "U.S. patent law" requires "naming of the actual inventors"). The MPEP explains that "if a determination is made that the inventive entity named in a U.S. application is not correct . . . a rejection should be made on this basis." *Id.* "As a critical requirement for obtaining a patent, inventorship is material." *PerSeptive Biosystems, Inc. v. Pharmacia Biotech, Inc.*, 225 F.3d 1315, 1321 (Fed. Cir. 2000).

37. Had the Examiner been apprised of the fact that the work in Example 13 was conceived of and performed by researchers at University College London, the Examiner would have required correction to the inventorship group and would not have issued the patent without such a correction.

38. Further, Natera made numerous other misrepresentations to the Patent Office during the prosecution of the '454 Patent.

39. First, in response to rejection in view of Forshew (2012), Natera argued as follows:

Furthermore, Forshew's TAm-Seq process was rationally and deliberately designed to rely on single-plex, "individual amplification to purify and select for intended targets" (pg. 3). In fact, Forshew had considered but dismissed multiplex targeted amplification - "Multiplex amplification using a large set of primers could result in nonspecific amplification products and biased coverage" (Fig. 1B, pg. 3). Forshew deliberately resorted to parallel single-plex amplification on Access Array, which physically separate individual primer pairs and individual reaction volumes to avoid issues such as nonspecific amplification and primer dimer formation. There was no reason or motivation for one of ordinary skill in the art to alter Forshew's TAmSeq process by substituting a step rationally and deliberately designed by Forshew for purpose of addressing the issue of nonspecific amplification, for a step already considered but dismissed by Forshew.

The Examiner allowed the claims in view of these arguments, among others.

40. This argument, however, misrepresents the teachings of Forshew (2012). Specifically, Forshew (2012) includes a preamplification step that is a multiplex amplification.

41. Second, Natera argued for allowance of claim 1 of the '454 Patent over Forshew (2010) on the basis of a claim limitation of a sequencing depth of at least 50,000 per target locus. As set forth in NeoGenomics's Opposition to Plaintiff's Motion for a Preliminary Injunction and the accompanying declaration of Dr. Brian Van Ness, however, such an addition would have been obvious to a person of ordinary skill in the art at the time of the alleged invention.

42. Specifically, the patent prosecution attorneys and those substantively working with them, including Tianran Yan and Ms. Doshi, submitted arguments to the Patent Office based on these misrepresentations on October 7, 2022 in the prosecution of the '454 Patent with the deceptive intent of obtaining claims that were not an inventive advance over the prior art. The single most logical inference for these misrepresentations was an intent to deceive to obtain patents overbroad claims that is further shown by the pattern of conduct alleged in this pleading.

43. Natera also committed inequitable conduct by including a claim in the application for the '454 Patent including "whole genome sequencing" based on Example 13. But Natera, including its patent prosecutors (including Tianran Yan and Ms. Doshi) and inventor Bernhard

Zimmerman know that Example 13 does not include “whole genome sequencing” and that there is no basis for stating it does.

44. The expansion of claim scope to cover whole genome sequencing was achieved with deceptive intent. Natera’s team knew that there is no actual disclosure of “whole genome sequencing” and sought such claims anyway. Given that Natera knew any reference to “whole genome sequencing” in the ’454 Patent was erroneous, the single more logical inference for including that claim scope is deceptive intent that is further shown by the pattern of conduct alleged in this pleading. Obtaining expanded claim scope to “whole genome sequencing” without true support in the patent disclosure is material to patentability.

45. NeoGenomics further incorporates by reference all arguments and evidence in support of a claim of inequitable conduct included in its as set forth in its Opposition to Plaintiff’s Motion for a Preliminary Injunction.

ELEVENTH DEFENSE – UNCLEAN HANDS

46. Natera’s patent infringement claims are barred in whole or in part under the doctrine of unclean hands.

47. Based on the business misconduct set forth in connection with NeoGenomics’ Tenth Defense related to inequitable conduct, Natera has engaged in unclean hands with respect to the ’454 Patent such that it is now unenforceable.

NEOGENOMICS’ COUNTERCLAIMS AGAINST NATERA

In support of its Counterclaims against Natera, NeoGenomics alleges as follows:

NATURE OF THE ACTION

1. In response to Natera's allegations in the Complaint, NeoGenomics seeks a declaratory judgment that it has not infringed the Asserted Patents, that the Asserted Patents are invalid, and that the '454 Patent is unenforceable under the Patent Laws of the United States, 35 U.S.C. § 271 *et seq.*

THE PARTIES

2. Natera is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at 201 Industrial Road, Suite 410, San Carlos, California 94070.

3. NeoGenomics is a corporation organized and existing under the laws of the State of Florida, with its principal place of business at 9490 NeoGenomics Way, Fort Myers, FL 33912.

JURISDICTION AND VENUE

4. The Court has subject matter jurisdiction over NeoGenomics' declaratory judgment counterclaims pursuant to 28 U.S.C. §§ 2201 and 2202.

5. The Court has personal jurisdiction over Natera because Natera consented to jurisdiction in this District by filing its Complaint in this action.

6. To the extent that venue is proper in the underlying patent infringement action, venue is also proper with respect to NeoGenomics' Counterclaims pursuant to 28 U.S.C. §§ 1391 and 1400(b) and because Natera consented to this venue by filing its Complaint in this action.

FIRST COUNT

(Declaration of Non-Infringement of U.S. Patent 11,530,454)

7. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-6 of its Counterclaims as though fully set therein.

8. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

9. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

10. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

11. NeoGenomics hereby seeks a declaration that NeoGenomics has not infringed and is not infringing any valid and enforceable claim of the '454 Patent.

12. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

SECOND COUNT

(Declaration of Non-Infringement of U.S. Patent 11,519,035)

13. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-12 of its Counterclaims as though fully set therein.

14. Natera has brought an action asserting the '035 Patent against NeoGenomics and has alleged that it is the legal owner of the '035 Patent.

15. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '035 Patent.

16. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '035 Patent.

17. NeoGenomics hereby seeks a declaration that NeoGenomics has not infringed and is not infringing any valid and enforceable claim of the '035 Patent.

18. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

THIRD COUNT

(Declaration of Invalidity of U.S. Patent 11,530,454)

19. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-18 of its Counterclaims as though fully set therein.

20. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

21. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

22. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

23. The claims of the '454 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations, and laws pertaining thereof.

24. NeoGenomics incorporates by reference and restates the preceding paragraph 2 of NeoGenomics' Second Affirmative Defense of Invalidity as though fully set forth herein.

25. NeoGenomics hereby seeks a declaration that the claims of the '454 Patent are invalid.

26. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FOURTH COUNT

(Declaration of Invalidity of U.S. Patent 11,519,035)

27. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-26 of its Counterclaims as though fully set therein.

28. Natera has brought an action asserting the '035 Patent against NeoGenomics and has alleged that it is the legal owner of the '035 Patent.

29. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '035 Patent.

30. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '035 Patent.

31. The claims of the '035 Patent are invalid for failing to comply with the provisions of the Patent Laws, Title 35 of the United States Code, including without limitation one or more of 35 U.S.C. §§ 101, 102, 103, 112, and/or 116, and/or the rules, regulations, and laws pertaining thereof.

32. NeoGenomics incorporates by reference and restates the preceding paragraph 2 of NeoGenomics' Second Affirmative Defense of Invalidity as though fully set forth herein.

33. NeoGenomics hereby seeks a declaration that the claims of the '035 Patent are invalid.

34. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

FIFTH COUNT

(Declaration of Unenforceability of U.S. Patent 11,530,454)

35. NeoGenomics incorporates by reference and restates the preceding paragraphs 1-34 of its Counterclaims as though fully set therein.

36. Natera has brought an action asserting the '454 Patent against NeoGenomics and has alleged that it is the legal owner of the '454 Patent.

37. Natera has alleged and continues to allege that NeoGenomics has directly, indirectly, and willfully infringed and continues to directly, indirectly, and willfully infringe one or more claims of the '454 Patent.

38. An actual controversy, within the meaning of 28 U.S.C. §§ 2201 and 2202, has arisen and exists between Natera and NeoGenomics concerning whether NeoGenomics has infringed and is infringing any valid and enforceable claim of the '454 Patent.

39. NeoGenomics incorporates by reference and restates the preceding paragraphs 12–24 of NeoGenomics' Tenth and Eleventh Affirmative Defenses of Inequitable Conduct and Unclean Hands as though fully set forth herein.

40. NeoGenomics hereby seeks a declaration that the claims of the '454 Patent are unenforceable due to inequitable conduct and unclean hands.

41. A judicial declaration is necessary and appropriate at this time so that the parties may proceed in accordance with their respective rights and duties determined by the Court.

RESERVATION OF RIGHTS

42. NeoGenomics expressly reserves the right to assert any additional defenses or counterclaims that may now exist or in the future may be available based on discovery and further factual investigation in this case.

DEMAND FOR JURY TRIAL

43. NeoGenomics hereby demands a trial by jury of all issues so triable in this action.

REQUEST FOR RELIEF

WHEREFORE, having fully answered the Complaint and having asserted Affirmative Defenses, and Counterclaims, NeoGenomics respectfully requests the following relief:

A. That this Court enter judgment on Natera's Complaint and NeoGenomics's Counterclaims in favor of NeoGenomics, against Natera, with Natera being awarded no relief of any kind in this action;

B. That this Court enter judgment and/or declarations that NeoGenomics does not infringe the Asserted Patents, that the Asserted Patents are invalid, and that the '454 Patent is unenforceable;

C. That this Court enter a judgment declaring this case exceptional under 35 U.S.C. § 285 and awarding NeoGenomics its attorneys' fees and prejudgment and post-judgment interest;

D. That this Court award NeoGenomics all of its costs of this action; and

E. That this Court grant such other and further relief as the Court shall deem just and proper.

Dated: October 20, 2023

Respectfully submitted,

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** Special Appearance Under Local Rule 83.1(d)*